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ECTOPIC OVARIAN DECIDUA WITHOUT PREGNANCY*

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The first report of decidual transformation outside of the uterine mucosa was made by Walker,[1] in 1887, who observed it in association with an extra-uterine pregnancy. Schmorl,[2] Hirschberg,[3] Rosenberger,[4] Meyer,[5] Geipel,[6,7] Shaw,[8] and Weller[9] have defined the anatomical extent of extra-uterine decidual formations and have discussed their nature and significance, especially in regard to endometriosis. Taussig[10] coined the term ectopic decidua to describe the phenomenon in its extra-mucosal locations, and ectopic decidua (viz., outside of the endometrium) has been noted in association with pregnancy in such diverse locations as the endocervical stroma, the subserosa of the corpus uteri and its ligamentous attachments, the endosalpinx, the serosal surfaces of the fallopian tubes, ovaries, omentum, vermiform appendix, small and large intestine, urinary bladder, and portions of the mesenteries. Meyer[5] stressed the rôle of healed, low-grade, and pre-existing inflammation, especially that associated with the formation of adhesions, in the sensitization of the tissues for the decidual response. Ectopic decidua in pregnancy has been observed in the umbilicus, in laparotomy and hysterotomy scars, and in association with adenomyosis and endometriosis. Weller[9] has pointed out that the regional distribution of the ectopic decidual response corresponds with the distribution of endometriosis. Geipel's[6,7] reports of 40 cases of decidual reactions in pelvic lymph nodes during pregnancy furnish additional evidence of the widespread distribution in the pelvis of tissues that respond to certain stimuli much as does the endometrial stroma. It is the consensus that such ectopic decidual transforma-

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tions occur to some extent in almost every pregnancy after the first trimester.

Decidual transformation in the absence of pregnancy is much less frequent. Under the terms Dysmenorrhoea membranacea and Decidua menstrualis,[11] this phenomenon has been described in the endometrium where it is accompanied by persistent bleeding and pain. Good illustrations of this lesion are presented in the report of Reinhart.[12] Te Linde and Henriksen[13] have furnished additional clinical and pathologic details of such endometrial transformations. Decidual transformation in both the endometrium and the ovary is observed with proliferative lesions of trophoblast, e.g., choriocarcinoma developing after hydatidiform mole or pregnancy, or arising extragenitally without antecedent gestation.

Ectopic decidual reactions in the absence of pregnancy have been reported previously. The report by Schereschewsky[14] of a decidual reaction in an adenomyoma of the rectovaginal septum in a 32-year-old woman must be discounted because of an abortion less than 2 weeks before biopsy. At laparotomy 3 months later for complete extirpation of the lesion, no decidual reaction was visible. The first convincing cases of ectopic decidua unrelated to pregnancy were those of Schiller,[15] who presented 3 unequivocal examples and one which he thought might represent a transitional stage in the development of the cellular response. The 3 clear-cut lesions were all associated with chronic adhesive salpingo-oophoritis. Examination of the excised uteri established the absence of pregnancy. Schiller concluded that ectopic decidua represented a transformation of the pelvic endothelium, i.e., that decidual cells were derived from the peritoneum itself. In a subsequent publication,[16] replying to the criticism of Ulesco-Stroganowa,[16a] who was of the opinion that the ectopic decidual cells were epithelioid and in no way different from the usual type of cell found in inflammatory infiltrates, Schiller added 3 more cases in which ectopic decidua was found on the surface of the ovary and in which the possibility of pregnancy was excluded by gross and microscopic examinations of the uterus.

Other examples of ectopic decidua in the absence of pregnancy have been described by Wallart.[17,18] In contrast to Schiller's observations of surgical material, Wallart's 7 examples were found at necropsy of postmenopausal women ranging from 56 to 88 years in age, 5 being over 70 years. Wallart noted decidual cells not only on the surface of the ovary but also in the loose, cellular centers of corpora albicantia. He accounted for the development of decidua without preg-

nancy in terms of complex neural and hormonal interrelationships among the pituitary body, breast, and ovary in the climacteric.

Shaw[8] found 8 examples of ectopic ovarian decidua in the absence of pregnancy in 33 cases in which oophorectomy had been done. The decidual reaction was observed in the premenstrual phase of the endometrial cycle.

Materials and Methods

Fourteen of the 16 cases presented in this report were received at the Armed Forces Institute of Pathology from federal sources. (One case was contributed by Dr. Frank W. Konzelmann, Emergency Hospital, Washington, D.C., and one by Dr. Emory D. Warner, State University of Iowa.) No special factors are known to have operated in their selection since the decidual reactions were noted as incidental findings in material contributed to the Armed Forces Institute of Pathology for other purposes. The material available for study consisted of the original slides as well as duplicates made from multiple paraffin blocks, formalin-fixed tissue in most of the cases, and clinical and descriptive data. Sections stained with hematoxylin and eosin were used for routine study. The only special methods used were silver impregnations for reticulum and McManus' periodic acid Schiff reagent with and without diastase digestion.

Report of Cases

Case 1 (A.F.I.P. Acc. 92225)

In 1943, a 36-year-old colored woman, gravida ii, para ii, underwent supracervical hysterectomy following a cervical biopsy which was interpreted as squamous cell carcinoma, grade I. No postoperative irradiation was given. Re-examination of the material during the course of this study revealed squamous cell carcinoma *in situ*. Nine years later (1952) recurrent vaginal bleeding prompted another biopsy of the cervix. Adenocarcinoma was found in the cervical stump. The patient was treated with 4,000 r. of x-ray radiation (skin dose) to the pelvis anteriorly and posteriorly as well as with 3,500 mg. hr. of radium by Ernst applicator. Three months later the cervical stump with its tumor, both fallopian tubes and ovaries, and numerous pelvic lymph nodes were excised.

No distinctive features were recognized in the examination of the excised tissue. Most of the anatomical landmarks were obliterated by the preceding irradiation. In the fixed state the ovaries and tubes were adherent to each other and were firm, shrunken pieces of tissue, each measuring less than 3 cm. in greatest dimension.

Microscopic examination showed both ovaries to be composed of dense fibrous tissue with many corpora albicantia. Patches of fibrotic ovarian stroma were recognizable. On the surface of each ovary there was patchy loosening of the stroma, and in some of these areas, rounded nests of decidual cells were seen. This alteration of the stroma was found both at free margins and underlying dense fibrous tubo-ovarian adhesions. The decidual cells were polygonal, contained a small, often eccentric nucleus surrounded by a slightly basophilic cytoplasm, and were loosely arranged in a myxoid matrix. In one section an adrenal cortical rest was found in the meso-

varium. In another section a round accumulation of hilar cells was identified. No corpus luteum was found in sections of either ovary.

Case 2 (A.F.I.P. Acc. 216150)

A 49-year-old woman, gravida ii, para i, abortus i(?), had complained of uterine bleeding of about 6 months' duration. She was treated with x-ray radiation of unstated amount without success. A presumptive clinical diagnosis of submucous leiomyoma of the uterus was made, and hysterectomy and bilateral salpingo-oophorectomy were done. It is inferred from the record that about 4 months elapsed between the last x-ray treatment and the operation.

The uterus contained a submucous leiomyoma approximately 4 cm. in diameter. No products of conception were seen. The ovaries were small, firm, and shrunken, measuring no more than 2.5 cm. in greatest dimension.

Most of the ovary was composed of corpora albicantia and medullary tissue. The cortex was thin and somewhat fibrotic. Along the free margin a few patches of loosened stroma, composed of polygonal decidual cells with clearly defined cell interfaces, were seen just below the surface in the cortex. Underlying this area of focal decidual transformation were the remains of a corpus luteum, with disorganized architecture and degenerating cells.

Case 3 (A.F.I.P. Acc. 260099)

A 51-year-old white woman in active menstrual life had complained of menometrorrhagia of 2 to 3 months' duration. Curettage of the endometrial cavity revealed a well differentiated adenocarcinoma. She was treated with 3,600 mg. hr. of radium inserted into the uterine cavity. Seven weeks after irradiation hysterectomy and bilateral salpingo-oophorectomy were performed.

Examination of the uterus revealed a small tumor covered by a membranous slough. The tumor was superficial and did not invade the myometrium deeply. No products of conception were found in the uterus. The fallopian tubes and left ovary were without notable gross lesions. A papillary projection less than 1 cm. in diameter was observed on the surface of the right ovary at the lateral pole.

Microscopic examination of the papillary structure in the right ovary showed that it was a serous papilloma. However, the lateral pole of the left ovary contained a central area composed of a few cystic spaces of small to medium size surrounded and traversed by a transformed stroma. The cystic spaces were lined by a single layer of columnar epithelial cells which resembled endometrial epithelium; an occasional length of epithelium contained vacuolated cells. The stroma of this area was composed of compactly arranged polyhedral decidual cells, with clear, faintly basophilic cytoplasm and well demarcated acidophilic cell boundaries. This decidual stroma extended between the cysts, and the lining of the cysts in some places rested upon such stroma. A few nests of decidual cells were found in the cortex a short distance from the cystic area. This lesion was interpreted as endometriosis with decidual transformation of the stromal component. Subjacent to this lesion, toward the medullary portion of the ovary, was a somewhat shrunken and disrupted corpus luteum.

Case 4 (A.F.I.P. Acc. 282199)

A cystic mass in the region of the right ovary was found on routine examination of a 43-year-old woman. At laparotomy, a cyst was removed from the right ovary and a biopsy was performed on a nubbin of tissue on the surface of the left ovary. The cervix was coned, the endometrial cavity curetted, and an appendectomy was done.

A mild degree of chronic cervicitis was found. The curettings showed the endometrium to be in the early secretory phase. No products of conception or evidence of recent pregnancy were found. The cyst in the right ovary was thin-walled, measured 8.5 cm. in diameter, and was a pseudomucinous cystoma. The appendix was fibrosed. The nubbin of tissue from the left ovary measured 0.7 by 0.5 cm., was composed of firm whitish tissue, and had a tiny cystic area, 0.2 by 0.1 cm., at its surface.

Microscopic examination of this fragment showed that most of it was normal ovarian cortex. The small cyst was lined by a layer of columnar epithelial cells resembling endometrial glandular epithelium or altered peritoneum of an inclusion cyst. Similar, smaller cystic spaces were found nearby. Adjacent to this area were a few delicate adhesions that formed a pannus-like coating over the ovarian surface. These adhesions were relatively free from inflammatory infiltration, only a few lymphocytes and plasma cells being present. The stroma of the adhesions was composed of polyhedral decidual cells which extended for a short distance into the ovarian stroma. Most of the decidual cells were loosely arranged and had indistinct cell borders, but in some foci they were closely packed and the cell borders were distinct. The surfaces of the adhesions were covered by a single layer of flat mesothelial cells, and the decidual cells lay subjacent to this single cell layer. The presence or absence of a corpus luteum in this ovary could not be determined from the data at hand. No corpus luteum was found in the opposite ovary.

Case 5 (A.F.I.P. Acc. 300087)

A 39-year-old Army nurse, gravida 0, had complained of menometrorrhagia since the removal of cervical polyps 3 years previously. Physical examination revealed an enlarged, nodular uterus. A hysterogram was interpreted as showing a submucous leiomyoma. At laparotomy both ovaries were adherent to the parietes, and "chocolate" cysts were found bilaterally. The entire uterus and adnexal masses from both sides were removed.

The uterus was small. The endometrium was smooth and uniform. A submucous nodule was present. Both ovarian masses and fallopian tubes were covered with rough, coarse adhesions. A cystic corpus luteum was recognized in the left ovary. Both ovaries were distorted considerably by cysts of small and medium size, some filled with chocolate material, others with clear fluid.

Microscopic examination showed the endometrium to be slightly hyperplastic and the submucosal nodule to be a leiomyoma. Both ovaries were diffusely involved by cystic endometriosis with old and recent hemorrhage, and scarring. The cystic corpus luteum in the left ovary displayed no unusual features. The right ovary contained a few regressing corpora lutea and corpora fibrosa, none of recent vintage. Three of these structures contained decidual cells. In one instance the decidual transformation was in the form of a radial band from the center toward the periphery of the corpus luteum; in the other two, it was in the form of a discrete patch of altered stroma. There was no evidence of decidua near the peritoneal surface in any of numerous sections. The decidual cells were clearly distinguishable from the adjacent regressing luteal cells.

Case 6 (A.F.I.P. Acc. 339991)

A 49-year-old white woman, gravida i, para i, underwent hysterectomy and bilateral salpingo-oophorectomy because of symptoms related to the menopause, including disturbed menstrual flow. There was severe cystic cervicitis. No products of conception or evidence of recent pregnancy were found in the endometrium. A few leiomyomas were seen in the myometrium. Chronic adhesive salpingo-oophoritis was noted.

Microscopic examination revealed a large corpus luteum in one ovary (side not stated). The surface of this ovary was covered by many fine and coarse adhesions with varying numbers of lymphocytes and plasma cells. In many areas these adhesions covered the ovarian surface like a pannus, producing entrapped lacunae lined by intact peritoneal mesothelium. Within these subperitoneal adhesions, many aggregates of decidual cells were found. These varied from clusters of a few cells to patches more than one low-power field in extent. On occasion, the decidual transformation extended into the cortex of the ovary. The decidual cells were morphologically characteristic and displayed some variety in form, arrangement, and tinctorial reaction. In some areas they were loosely arranged in an edematous, myxoid matrix; in other areas the cells were in close apposition, with acidophilic boundaries sharply delimiting individual cells. The cytoplasm of some of the cells was strikingly opalescent. In the absence of decidual transformation, the cortex of the ovary was thick and cellular.

Case 7 (A.F.I.P. Acc. 538037)

A 35-year-old woman, gravida 0, para 0, had complained of postmenstrual vaginal discharge. Biopsy of the cervix revealed infiltrative squamous cell carcinoma. She was treated with 7,740 mg. hr. of radium and 8,000 r. of x-ray radiation (skin dose) to the pelvis anteriorly and posteriorly. Hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection were performed 10 weeks after radiation therapy was completed.

The uterus measured 7 by 4 cm. Residual tumor was seen in the cervical canal. No products of conception were found in the endometrium. Two leiomyomas were present in the myometrium. The right fallopian tube was dilated and contained purulent material. The right ovary measured 2.5 by 2 cm., and was smooth, glistening, and appeared to be replaced by a firm, white, friable tissue. The left tube and ovary were similar in appearance to the right.

Microscopic examination revealed residual squamous cell carcinoma in the cervix. The endometrium was in a proliferative phase. The fallopian tubes showed acute follicular salpingitis and pyosalpinx. On and below the peritoneal surface of one ovary and above a disorganized corpus luteum, a few small patches of decidual cells were loosely arranged in an edematous matrix. Additional blocks from both ovaries failed to reveal any more decidua.

Case 8 (A.F.I.P. Acc. 546894)

A 27-year-old white woman, gravida 0, para 0, had complained of irregular vaginal spotting. Biopsy of the cervix revealed infiltrating squamous cell carcinoma. She was treated with 7,740 mg. hr. of radium and 7,200 r. of x-ray radiation to the pelvis anteriorly and posteriorly. Hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection were done 12 weeks after irradiation therapy was completed.

The uterus measured 7.5 by 4 by 1.5 cm. The cervix was covered by smooth epithelium. The endometrial cavity was smooth and regular. No products of conception were identified. The ovaries were small, but normal in contour.

Microscopic examination failed to reveal any residual squamous cell carcinoma. The endometrium was in a proliferative phase. There was a diffuse radiation effect throughout the fallopian tubes, uterus, and ovaries. A cystic corpus luteum was present in one ovary, compressing the overlying cortex. On the peritoneal surface near this structure a fairly extensive decidual transformation which extended into the cortex was associated with a minimal inflammatory reaction consisting of scattered lymphocytes and a few delicate fibrous tags at the surface. On the peritoneal

surface of the other ovary there was a less conspicuous decidual change not associated with inflammation. A similar reaction was found on the surface of the mesosalpinx in an area of fibrosis with focal psammoma body formation.

Case 9 (A.F.I.P. Acc. 555513)

A 33-year-old white woman, gravida v, para iv, had complained of pain in the right side associated with menometrorrhagia of 7 months' duration. Examination revealed a firm, fixed mass, 5 cm. in diameter, in the right adnexal area. The uterus, both fallopian tubes, and left ovary were described in the surgeon's note as normal. A right salpingo-oophorectomy was performed.

The fallopian tube was kinked and tortuous. The ovarian tissue measured 5.5 by 3.5 cm. and was densely adherent to the tube. It was composed of a fairly well demarcated mass of yellowish gray tissue surrounded by a zone of recognizable ovarian cortex in which a corpus luteum was identified.

The mass within the ovary consisted of a dense mixture of lymphocytes, plasma cells, and histiocytes with occasional eosinophils and polymorphonuclear leukocytes filling a large abscess cavity. The inflammatory lesion involved chiefly the medulla, but patches of exudate and edema disrupted the cortex. The peritoneal surface was covered with coarse adhesions. In only one of many sections did a few of these adhesions contain small nests of decidual cells with sharp borders. A small corpus luteum was disrupted by the diffuse inflammatory reaction. The fallopian tube exhibited subacute adhesive salpingo-oophoritis.

Case 10 (A.F.I.P. Acc. 564300)

A 65-year-old woman, gravida ii, para i, had complained of painless vaginal bleeding of 2 years' duration. The uterus was enlarged to twice normal size. Curettage revealed a fairly well differentiated adenocarcinoma of the endometrium. A hysterectomy and bilateral salpingo-oophorectomy were performed 9 days later. There was no mention of any radiation therapy before operation.

The uterus measured 11.5 by 7.2 by 6.5 cm. The endometrial cavity contained a large friable mass of yellowish and reddish tissue. The fallopian tubes were not remarkable. Both ovaries were small and firm, the left measuring 2.7 by 1.2 by 0.8 cm.; the right, 1.4 by 1.1 by 0.8 cm. Numerous corpora albicantia and a white nodule measuring 0.6 by 0.5 by 0.3 cm. on the surface of the right ovary were noted.

Microscopic examination confirmed the presence of an endometrial adenocarcinoma which invaded the myometrium. An area of cortical fibrosis corresponding to the small nodule seen grossly and a few delicate fibrous adhesions free from inflammatory cells were seen in the right ovary. The central portion of both ovaries was occupied by large and small corpora albicantia. In the cortex near the surface of the left ovary above the corpora albicantia there was a zone of decidual cells which were irregularly dispersed, and associated with a scanty infiltration of lymphocytes and an occasional eosinophil. No corpus luteum was identified in the vicinity. A few delicate fibrous adhesions were present nearby, but these did not contain decidual cells.

Case 11 (A.F.I.P. Acc. 574297)

A 40-year-old white woman, who had had a radical mastectomy 1 month previously for carcinoma of the breast with lymph node metastases, was treated further by hysterectomy, bilateral salpingo-oophorectomy, and appendectomy.

The uterus measured 6 by 4 by 3 cm. No gross abnormalities of the uterus, fallopian tubes, ovaries, or appendix were observed. No products of conception were found in the endometrium, which was in a proliferative phase. Both ovaries showed

distortion and scarring secondary to diffuse endometriosis and healed adhesive perioophoritis. They contained several small cysts, lined in part by endometrium-like epithelium and in part by endometrial stroma-like tissue admixed with granulation tissue and hemosiderin-laden macrophages. No fresh corpora lutea were found in either ovary, but numerous corpora fibrosa and albicantia were present in the medullae. The overlying cortices were thinned and scarred. In the medulla of one ovary immediately beneath a cortical scar was a corpus albicans with a loose and fibrous center which contained many hemosiderin-laden macrophages. At the margin of this corpus albicans was a single patch of compactly arranged decidual cells with polygonal outlines, pale basophilic cytoplasm, vesicular nuclei, and sharply defined cell borders. This patch was made up of less than 40 decidual cells and a few lymphocytes and it could not be detected in further sections prepared from the original paraffin block. In multiple sections from this ovary another patch of decidual cells, slightly smaller than the first, was found adjacent to a corpus albicans near the corticomedullary junction.

Case 12 (A.F.I.P. Acc. 512572)

A 42-year-old white woman had complained of severe menorrhagia and dysmenorrhea of 6 months' duration. Hysterectomy and right salpingo-oophorectomy were performed. The uterus measured 8.5 by 5.5 by 4 cm. and contained several small, spherical leiomyomas. The endometrial cavity was lined by smooth epithelium; no products of conception were identified. The right fallopian tube was not remarkable. The right ovary measured 4 by 3 by 2 cm. and contained several corpora lutea of varying ages, including a recent one with a central cavity filled with gelatinous material.

Microscopic examination showed the uterus to be lined by endometrium in an early secretory phase. The tumors in the myometrium proved to be leiomyomas. No lesions were present in the fallopian tube. Arising from the surface of the ovary above a large corpus luteum and separated from it by a layer of compressed ovarian cortex was a single, delicate, fibrous adhesion packed with swollen, polyhedral decidual cells. The nuclei were small, often eccentric, and relatively clear. The cytoplasm was slightly basophilic and the cell borders sharply demarcated. In several blocks taken from this ovary only a rare, delicate, fibrous adhesion was encountered at the surface. In one of these, also not far distant from the corpus luteum, a few decidual cells were identified.

*Case 13 (A.F.I.P. Acc. 582760)**

A 48-year-old woman, gravida 0, had complained of severe menorrhagia of over 1 year's duration. Ten years previously a right salpingo-oophorectomy had been performed. No history of endocrine therapy was elicited. At laparotomy the right fallopian tube and ovary were absent; the left fallopian tube also was absent. The omentum, small bowel, colon, and uterus were bound together in a mass of adhesions. The uterus, left ovary, and a portion of omentum were removed.

The uterus measured 5.5 by 5 by 3.5 cm. Its serosal surface was diffusely roughened and numerous shaggy adhesions were present. The myometrium contained a small leiomyoma. The endometrium was smooth and thin; no products of conception were present. The left ovary measured 3 by 2.5 by 1.5 cm., and a few adhesions were seen at its surface. Also noted on the surface were several irregularly dispersed, small, whitish elevations less than 1 mm. in diameter. At one pole of the ovary there was a corpus luteum about 0.6 cm. in diameter.

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* Contributed by Dr. Frank W. Konzelmann, Emergency Hospital, Washington, D.C.

The endometrium was in a proliferative phase. Diffuse, chronic perimetrosalpingo-oophoritis was present. Beneath the peritoneal surface and extending into the substance of the ovarian cortex were many clusters of cells which were characteristic of decidua. These cells tended to be arranged in spherical nests but also had diffused into the cortex. The decidual reaction was greatest near the corpus luteum, but several nests of decidua were present in sections some distance from this structure. Many of the foci of decidual reaction were associated with peritoneal adhesions. The decidual response in this case was more extensive than in any other of this series.

*Case 14 (A.F.I.P. Acc. 580367)**

A 44-year-old woman, multigravida, had complained of irregular vaginal bleeding for 2 years. A curettage was performed and a diagnosis of adenocarcinoma of the endometrium was made. The patient received 4,800 mg. hr. of radiation. One month later, panhysterectomy and bilateral salpingo-oophorectomy were performed. The pertinent diagnoses were adenocarcinoma of endometrium, with radiation changes, and pseudomucinous cystadenoma of the ovary. In the opposite ovary, a regressing corpus luteum was found. Adjacent to this on the ovarian surface, a microscopic focus of about 20 typical decidual cells was seen. Another nodular collection of similar cells lay immediately beneath the ovarian surface adjacent to a small zone of hemorrhagic peri-oophoritis.

*Case 15 (A.F.I.P. Acc. 582924)**

A 42-year-old woman, gravida i, para i, had complained of menometrorrhagia for 9 months. Curettage of the endometrium revealed adenocarcinoma. Panhysterectomy and bilateral salpingo-oophorectomy were done 7 weeks after intracavitary irradiation. Sections of the uterus contained areas of adenocarcinoma of the endometrium with irradiation changes. One ovary contained a cystic corpus luteum. On and just beneath the ovarian surface, three minute foci of well preserved decidual cells with loose myxoid stroma were noted. They were covered by a thin inflammatory membrane containing a few lymphocytes. A small nodule of typical interstitial cells was seen in the hilus of the ovary.

Case 16 (A.F.I.P. Acc. 604713)†

A 64-year-old nulliparous white widow was admitted with cardiac failure of moderate severity. Menopause had occurred 15 years previously. A large cystic mass in the region of the left ovary extended out of the pelvis almost to the umbilicus. The patient admitted having been aware of this mass for only 2 or 3 months. At laparotomy a loculated cyst involving the left ovary was found and approximately 1,200 cc. of clear fluid were evacuated. The uterus was small and knobby, with numerous leiomyomas. A "chocolate cyst" involved the right broad ligament and right ovary.

The lining of the left ovarian cyst was smooth and shiny and showed no adenomatous areas. Microscopic examination revealed leiomyomas and adenomyosis of the corpus uteri and endometriosis of the ovaries. A few scattered foci composed of large, pale-staining cells typical of decidual tissues were found in the ovaries but were not associated with the areas of endometriosis.

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Summary of Pathologic Changes

The ectopic decidual reaction was located immediately subjacent to the peritoneal surface and in close proximity to a recent corpus luteum (frequently disrupted) in 8 cases (cases 2, 3, 6, 7, 8, 9, 12, and 13). In case 1, no corpus luteum was found; an adrenal rest was present in the mesovarium and a nest of hilar cells was found in the medulla of the ovary. A similar hilar cell nest was present in case 15. In case 4, the presence or absence of a corpus luteum could not be determined. In case 5, the decidual reaction was in a regressing corpus luteum and also in corpora fibrosa and albicantia; a recent corpus luteum was present in the opposite ovary. In case 9, the decidual reaction consisted of one small focus of transformed cells some distance from the corpus luteum. In case 11, the decidual reaction also consisted of two small foci of cells, each adjacent to a corpus albicans in which no functioning luteal cells were identified. In case 12, the decidual reaction was limited to two small peritoneal adhesions near a normally formed, fresh corpus luteum.

Periovarian adhesions of a postinflammatory nature were present to a significant extent near the ectopic decidual reaction in 14 of the 16 cases, and the reaction was located both in the adhesions and in the cortex just below them. A history of recent radium or x-ray treatment to pelvic structures was given in 9 of the 16 cases. In 5 cases the decidual reaction was associated with endometriosis; in one of these there was a history of previous irradiation.

Cases 10 and 16 are exceptional in this series in that there was no corpus luteum, no previous irradiation, and no significant inflammatory adhesions. In case 16 an old "chocolate" cyst, presumably endometrial, was found in the ovary. These 2 cases closely resemble those reported by Wallart.[17,18]

The uterus was available for examination in 15 of the 16 cases. No evidence of pregnancy or of recently terminated pregnancy was found in any of them. In case 9, the uterus was not available for study, but was reported as normal in the surgeon's notes. There is nothing in the antecedent or subsequent history of this patient to suggest pregnancy.

The identification of cells as decidual rests upon their resemblance to the decidual cells seen in the endometrium during the late progestational stage of the menstrual cycle and in pregnancy. Weller's[9] description of ectopic decidual cells is an adequate standard: "nests of large cells with slightly basophilic cytoplasm and spherical, usually

eccentric, nuclei, ... often 30 microns or more in diameter." To this description might be added the generally polygonal shape of the cells, their tendency to form compact pavement-like tissue simulating the stratum compactum or, alternatively, a looser meshwork simulating the stratum spongiosum of the decidua vera, and the frequent refractile acidophilia of the intercellular substance. The cells observed in the ovary in these 16 cases satisfy these morphologic criteria.

Geipel[7] pointed out that decidual cells, whether in the endometrium or in ectopic location, contain glycogen. In 14 of the 16 cases in this series, material was available for treatment with the periodic acid-Schiff (PAS) method. In each of these 14 cases Schiff-positive material was found both as an intensely colored zone of fuchsinophilic material condensed at the peripheral portion of the cells in question and as inconstant smaller particles in the relatively clearer perinuclear zone. Parallel sections digested with diastase showed that this material was not completely digested. Although the particles in the perinuclear areas were blanched, traces of the fuchsinophilic material remained at the cell border. The most striking illustration of this partial digestion was in case 13. Whether this observation indicates the presence of small amounts of mucopolysaccharide along with the larger moiety of glycogen cannot be determined. Shaw[8] stressed the value of demonstrating argyrophilic intercellular fibers between decidual cells to distinguish them from swollen cells which might simulate decidua. In the same 14 cases, sections treated by Gridley's reticulum method showed delicate, often intertwined, intercellular fibrils upon which silver had been deposited.

The identification of the two patches of decidua in case 11, and the decidua in the two delicate peritoneal adhesions in case 12, was made by comparison with the appearance of similar cells found in the other 14 cases in routine hematoxylin and eosin preparations. The quantity of decidua in these two cases was not sufficient to permit the use of periodic acid and silver impregnation techniques. In case 16, only sections stained with hematoxylin and eosin were available for study.

Discussion

The cells which are transformed into decidual cells in response to appropriate stimuli are stromal in origin and derived from the subcelomic mesenchyme, the same embryonic tissue from which the endometrial stroma develops. In the ovary this tissue is represented by an inconspicuous layer of cells directly beneath the peritoneal surface which blends imperceptibly with the ovarian cortex. This

accounts for both the gross appearance of the lesions, "small nodules, streaks and patches produced by a thickening of the serosa or, more properly, the subserosa" (Weller[9]), and the microscopic observations described above. In the early embryo, this subcelomic mesenchyme surrounds both the wolffian and müllerian ducts in the urogenital ridge. The two ducts are in close proximity at the time of their formation as evaginations from the celomic lining, and it is not surprising that occasionally a kidney removed during pregnancy should display a decidual reaction in the renal pelvis, as described by Bettinger.[19] The capacity to be transformed into decidua under appropriate conditions is an inherent and unique property of the mesenchyme of the urogenital ridge and its derivatives.

The conditions under which, and the mechanisms by which, this transformation occurs are generally constant, but can vary within certain limits. Pregnancy is the usual condition in which decidua develops, either in the endometrium or ectopically, presumably as the response to progesterone elaborated by the corpus luteum and the syncytiotrophoblast. However, decidua can develop physiologically in the absence of pregnancy, i.e., without trophoblast. The predecidua in the endometrium from the 23rd through the 28th day of the hypothetically normal menstrual cycle is cytologically indistinguishable from true decidua; the only difference is quantitative. Conversely, decidua may develop both in the endometrium and ectopically in association with lesions of trophoblast, notably choriocarcinoma. In such cases it is presumed that the decidual transformation is not the result of the direct stimulus of the chorionic gonadotropin but is mediated through the intervening stimulus of luteinized theca cysts in the ovary. These respond to the APL substance in the trophoblast by liberating an excessive amount of progesterone, which, in turn, is the stimulus for formation of decidua. The failure to observe decidual reactions beneath the peritoneal surfaces in males with choriocarcinoma, genital or extragenital, is added evidence that the intermediate position of the lutein cell and the progesterone it elaborates is a necessary link in the chain.

Loeb[20] originally produced deciduomas in the uteri of guinea-pigs by non-specific trauma during the lutein phase of the estrous cycle. This reaction occurred only during the active phase of the corpus luteum, and it was clear that the synergistic actions of local trauma and progesterone were the essential conditions for this phenomenon. Subsequent observations by a number of investigators have confirmed Loeb's results. Notable among these are the investigations of Unter-

berger,[21] who produced ectopic deciduomas in the uterine serosa of virgin rabbits by making incisions in the serosa, then mating the rabbit. Goldstein and Tatelbaum[22] were able to produce deciduomas in guinea-pigs by injecting an alcoholic extract of rabbit corpus luteum. The decidual transformations which they produced were both in the endometrium and beneath the uterine serosa following incisional trauma. Recently Stuermer and Stein[23] demonstrated that endometrium grown *in vitro* assumes the fibroblastic form when grown in ordinary media, but assumes an epithelioid shape, much like sheets of decidual cells, when grown in a medium enriched by serum from umbilical cord.

In the present series the ectopic decidua in all but 4 cases (cases 1, 10, 11, and 16) was found in close proximity to either an active corpus luteum anatomically damaged by ionizing irradiation or other inflammatory process, or one in some stage of regression. In those cases in which the ectopic decidua was not at the surface of the ovary or in inflammatory adhesions at the surface (cases 5 and 11), the presence of subcelomic mesenchymal cells is explained by mechanical transportation of these cells during the cycle of follicle rupture, luteinization, and involution, much as peritoneal cells may be drawn into the substance of the ovary. In all but 2 cases, either a recent and active or an old and healed inflammatory reaction involved the ovarian surface. Ionizing irradiation therapy for a variety of gynecologic complaints was often sufficient to traumatize the stromal cells so that they would respond to the hormonal stimulus. Lacassagne, Fehr, and Nyka[24] demonstrated the formation of uterine deciduoma in rabbits following doses of x-ray sufficient to kill ova but insufficient to destroy corpora lutea.

Cases 1, 10, 11, and 16 differ from the other cases in this series in that no corpus luteum, either active or involuting, was present in either ovary. In cases 10 and 16 the patients were chronologically postmenopausal; in case 1, radiation therapy for adenocarcinoma of the cervix had been given more than 3 months previously, and not even disorganized luteal structures remained subjacent to the decidual reaction as in cases 4, 8, and 9. A source for the progesterone or progesterone-like stimulus other than the corpus luteum must be postulated in these cases. The clue furnished by the observation of an adrenal cortical rest in the mesovarium in case 1 implicates the adrenal cortex as a possible source; the hilar cell nest does not seem to be a likely source of progesterone. Engelhart[25] was able to induce progestational changes (secretion and formation of decidua) in the

endometrium of virgin rabbits by injecting a lipidic extract of the human adrenal cortex. Callow and Parkes[26] confirmed and extended the observations of Engelhart to include extracts from the adrenal glands of cattle, horses, pigs, and sheep. Beall[27] isolated progesterone as a chemically pure substance from the adrenal cortex of oxen. However, progesterone is not unique among steroid hormones in its ability to produce progestational effects. McKeown and Zuckerman[28] produced a deciduoma in 1 of 6 rats injected with testosterone as well as progestational changes in the endometrium. However, they attributed the decidual response to the numerous corpora lutea which were present in the ovary. Leathem and Crafts[29] produced progestational changes in the endometrium of spayed, adrenalectomized cats with desoxycorticosterone acetate, but did not attempt to produce deciduomas. Whether the source of the progesterone-like stimulus in case 1 was actually from the adrenal rest or from the adrenal cortex is conjectural. In neither case 10 nor case 16 was an adrenal rest found, and it is presumed that the decidual response was produced by progesterone elaborated in the adrenal cortex. It is also presumed that the occasional observation of decidual cells in the ovaries of postmenopausal women in whom no functioning corpus luteum remains can be explained on this basis. In none of these cases was adrenal or pituitary tissue available for study.

Summary

Sixteen examples of ectopic decidual reaction in the ovary in the absence of current or recent pregnancy are described.

In 14 of the 16 cases a functioning corpus luteum which had undergone disruption was present nearby; in one case the presence or absence of a corpus luteum could not be determined. An adrenal rest but no corpus luteum was observed in one case and in 2 cases nests of hilar cells were seen.

Periovarian adhesions were present in 14 cases; radiation therapy had been given in 9 cases; endometriosis was an associated condition in 5 cases.

The decidual reaction is defined as an inherent and unique property of the mesenchyme of the urogenital ridge and its derivatives. In the ovary the transformation usually occurs in an inconspicuous layer of cells normally located just below the mesothelial surface.

Decidual reactions in the absence of pregnancy are similar to experimentally produced deciduomas.

The decidual response follows stimulation of appropriate cells by

progesterone or progesterone-like substances elaborated usually in the corpus luteum, but in its absence, possibly in the adrenal cortex.

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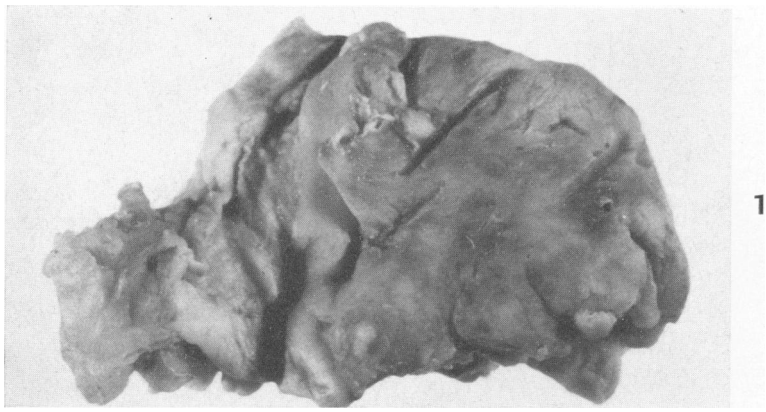
LEGENDS FOR FIGURES

FIG. 1. Case 13 (Armed Forces Institute of Pathology Acc. 582760). Elevated decidual nodules on ovarian surface. × 4½.

FIG. 2. Case 4 (A.F.I.P. Acc. 282199). Decidual cells in polypoid formation. Hematoxylin and eosin stain. × 150.

FIG. 3. Case 8 (A.F.I.P. Acc. 546894). Small nest of decidual cells adjacent to disintegrating corpus luteum. Hematoxylin and eosin stain. × 125.



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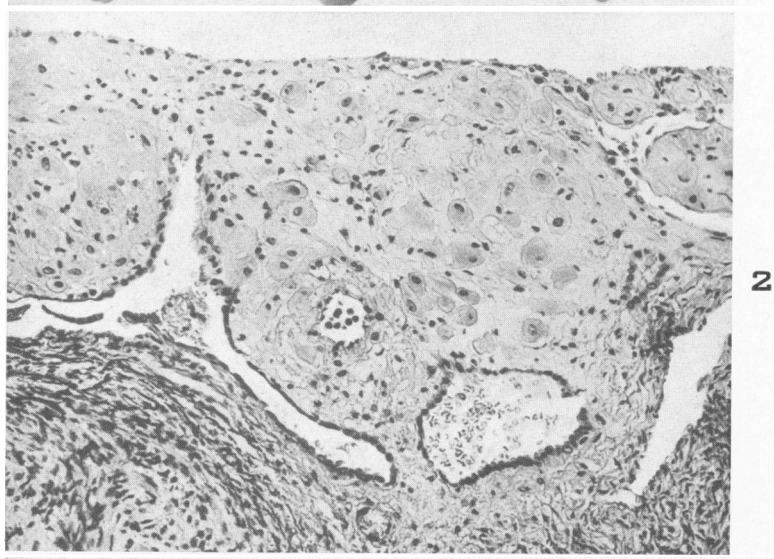

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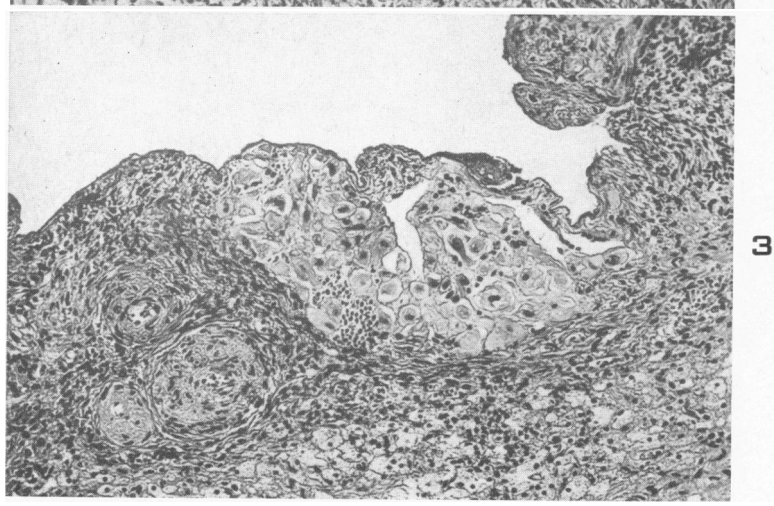

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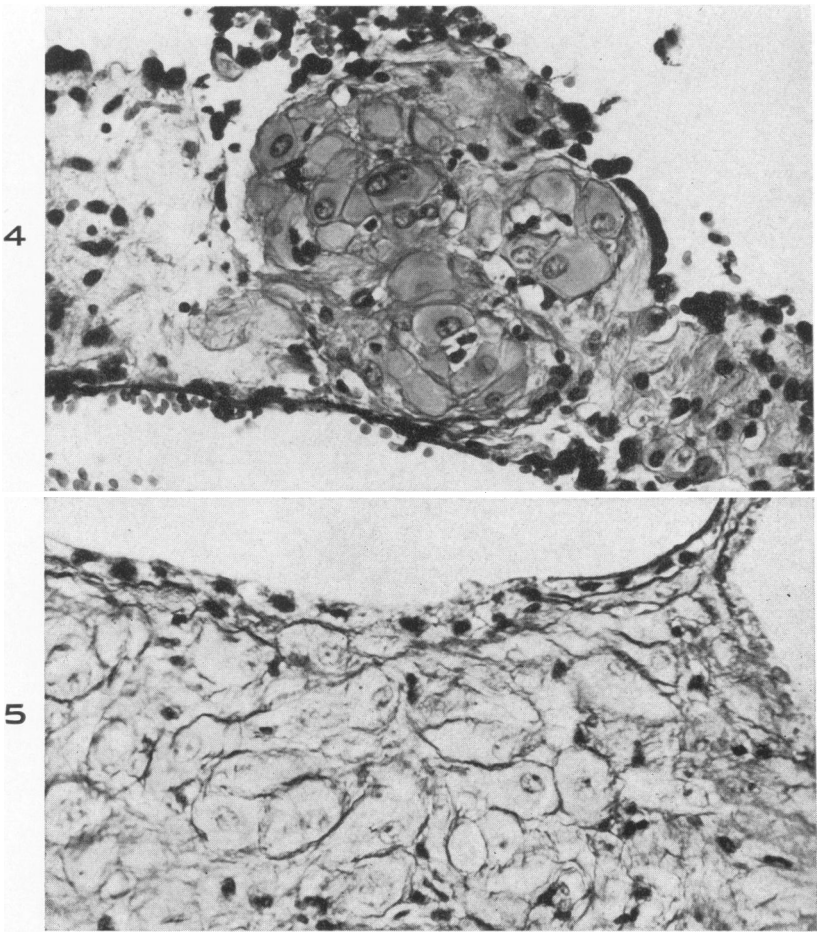


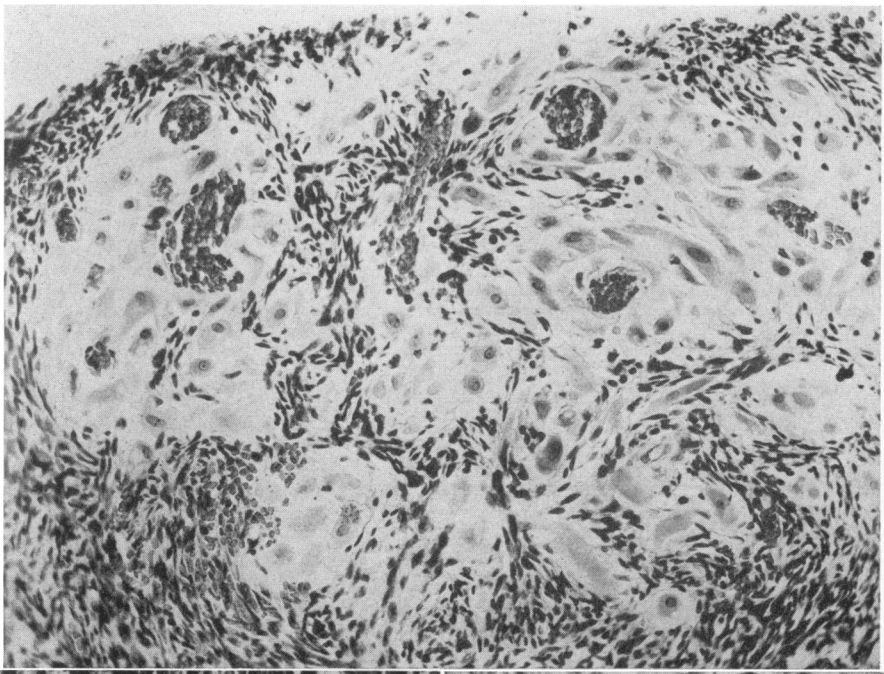
FIG. 4. Case 9 (A.F.I.P. Acc. 555513). Nest of decidual cells in inflammatory pannus. Periodic acid-Schiff (PAS) stain. × 275.

FIG. 5. Case 3 (A.F.I.P. Acc. 260099). Decidual cells are outlined by reticulum. Gridley's reticulum stain. × 300.

FIG. 6. Case 13 (A.F.I.P. Acc. 582760). Nest of decidual cells in cortical stroma. Hematoxylin and eosin stain. × 200.

FIG. 7. Case 10 (A.F.I.P. Acc. 564300). Scattered decidual cells in cortical stroma. Hematoxylin and eosin stain. × 300.

FIG. 8. Case 10 (A.F.I.P. Acc. 564300). The same group of cells as shown in Figure 7 with Schiff-positive outlines. PAS stain. × 350.



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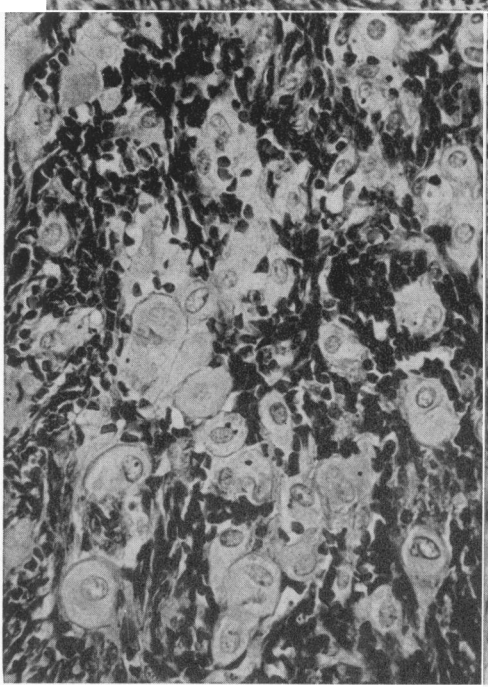

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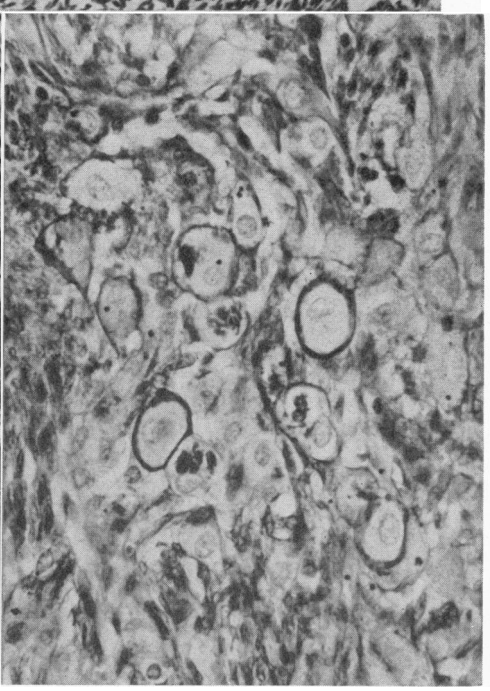

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